

Beyond Intra-Base-Pair Hydrogen Bonds in DNA Structures: A Comprehensive Analysis

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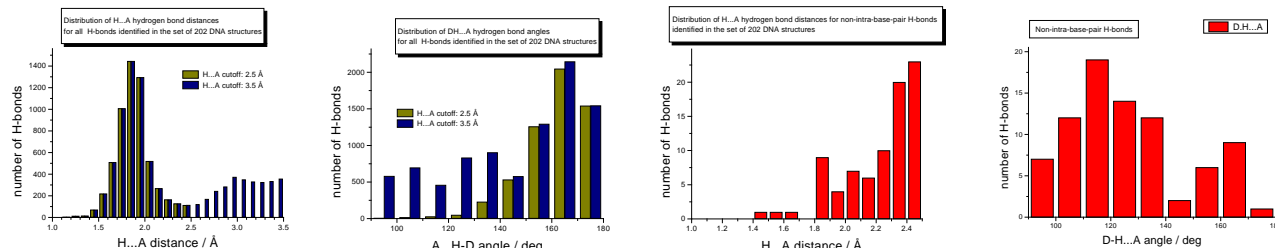
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Introduction

Hydrogen bonding in Watson-Crick pairs is of utmost importance for the structure of DNA. From the increasing number of structural studies on DNA we have learned, however, that this standard view of hydrogen bonding in DNA has to be supplemented by hydrogen bonding interactions of the non-Watson-Crick type, usually called *mismatches* or *non-canonical pairings*. In studies on the tracts of DNA dodecamers Nelson et al. (*Nature*, 1987, 330,221) and Coll et al. (*PNAS* 1987, 84, 8389) have identified for the first time *cross-strand diagonal H-bonds*. They represent a third type of H-bonds in DNA structures because they connect different base-pairs. These *inter-base-pair-hydrogen bonds* have been claimed to contribute to a particular stability and rigidity of AT tracts in DNA. In order to gain deeper insight into the importance of this type of H-bonds for DNA we have performed a systematic search for *non-intra-base-pair hydrogen bonds* in a set of 202 DNA structures from the Protein Data Bank.

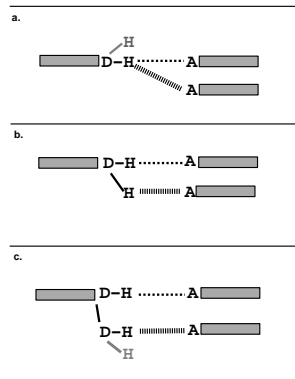
Results

Distributions of geometrical H-bond parameters



H-bond motifs with non-intra-base-pair H-bonds

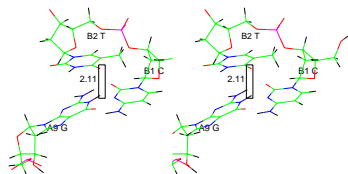
General motifs



A table of all non-intra-base-pair H-bonds can be obtained here.

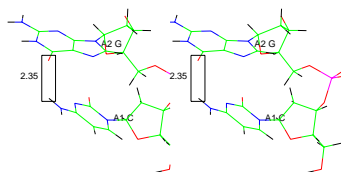
A-DNA (PDB code: 1dn6) base-base inter-strand H-bond

VRML format



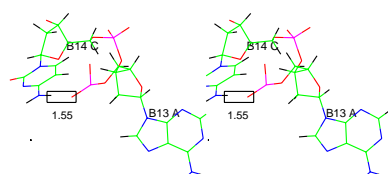
DNA-bisintercalator complex (PDB code: 108d) base-base intra-strand H-bond

VRML format



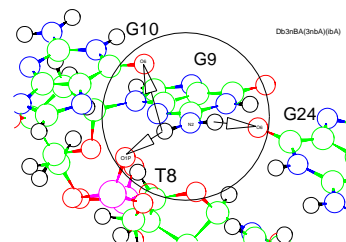
Telomeric DNA (PDB code: 200d) base-backbone intrastrand H-bond

VRML format



Telomeric DNA (PDB code: 186d) Motif with two non-intra-base-pair H-bonds

VRML format



Statistics of non-intra-base-pair H-bonds in DNA structures

Total number of non-intra-base-pair H-bonds:	82	
Three center H-bonds with one or two non-intra-base-pair H-bonds:	36	
Two-center H-bonds:	46	
Base-backbone H-bonds:	24	
Base-base H-bonds:	58	
Number of H-bonds for residue types:		
donor acceptor		
A G	29	
G G	11	
G C	8	
G T	6	
G A	6	
C T	5	
C G	4	
A G	3	
C A	3	
T A	2	
T C	2	
T G	2	
A A	1	
T T	1	
Donor atoms:	Acceptor atoms:	
A:N6	T:O4	32
G:N2	G:O3	10
C:N4	C:O2	6
G:N1	T:O2	6
T:N3	A:O2P	5
	G:O2P	4
	A:O4*	3
two-H donor atoms:	C:O4*	3
(A:N6, C:N4, G:N2):	G:O3*	3
	T:O4*	2
one-H donor atoms:	A:N1	2
(G:N1, T:N3)	G:N3	1
	C:O1P	1
	A:O1P	1
	A:N7	1
	G:O4*	1
	T:O1P	1
Fraction of structures with non-intra-base-pair H-bonds:		
A-DNA	14%	
B-DNA	18%	
Z-DNA	18%	
unusual DNA	26%	
DNA-drug complexes	18%	
DNA-protein complexes	42%	

DNA structures from the Protein Data Bank searched for non-intra-base-pair hydrogen bonds

A-DNA (14 structures):
X-ray: 115d, 137d, 160d, 172d, 197d, 1ana, 1d91, 1d92, 1dn6, 218d, 221d, 2ana, 2d47, 3ana
B-DNA (49 structures):
X-ray: 111d, 112d, 113d, 114d, 118d, 122d, 123d, 126d, 150d, 153d, 158d, 167d, 178d, 194d, 196d, 1bdn_AB, 1bdn_CD, 1bna, 1cgc, 1d23, 1d27, 1d28, 1d29, 1d49, 1d56, 1d57, 1d60, 1d65, 1d75, 1d77, 1d80, 1d81, 1d89, 1d97, 1d98, 1d99, 1da3, 1dn9, 1dnm, 1ndn_ABC, 1ndn_TUV, 2bna, 2d25, 3bna, 4bna, 4dnb, 7bna, 9bna
NMR: 175d
Z-DNA (23 structures):
X-ray: 131d, 133d, 145d_AB, 145d_CD, 180d, 181d, 1d24, 1d39, 1d40, 1d41, 1d48, 1d53, 1d76, 1da1, 1da2, 1dgc, 1dn4, 1dn5, 1dn8, 1dnf, 1zna, 223d, 2dgc
Other DNA structures (27 structures):
X-ray: 190d, 191d, 192d, 1d16, 1d31, 1d59, 200d, 208d, 241d
NMR: 103d, 105d, 106d, 134d, 136d, 139d, 143d, 149d, 156d, 177d, 179d, 186d, 1d18, 1d19, 1d20, 1d70, 1da4, 201d
DNA-drug complexes (49 structures):
X-ray: 101d, 102d, 109d, 121d, 127d, 128d, 129d, 130d, 144d, 154d, 166d, 162d, 195d, 198d, 1d21, 1d22, 1d30, 1d32, 1d43, 1d44, 1d45, 1d46, 1d63, 1d64, 1d86, 1dne, 1dnh, 1f9g, 1fex, 1fey, 1ppr, 209d, 224d, 227d, 2d4d, 2d55, 2d56, 2d58, 2d59, 2dnd, 5bna, 6bna, 8bna
NMR: 107d, 108d, 146d, 185d, 193d, 199d, 202d
DNA-protein complexes (40 structures):
X-ray: 1apl, 1brn, 1cgp, 1cma, 1d66, 1dct, 1dgl, 1gku, 1hdd, 1hcr, 1hut, 1kin, 1li, 1mb, 1mdy, 1oct, 1par, 1per, 1pdh, 1pvi, 1pyi, 1rpe, 1rva, 1rvb, 1rvd, 1rvs, 1ro, 1ysa, 1ytb, 1zaa, 2bpf, 2bpg, 2dnj, 2drp, 2orf, 2rve, 3cro
NMR: 1gat, 1gat, 1me1, 1mse
Structures for which non-intra-base-pair H-bonds were found are given in bold.

Summary

A set of 202 DNA structures was scanned for non-intra-base-pair H-bonds. We could identify 82 H-bonds of this type in 44 structures. This corresponds to a fraction of about 1.4% as compared to the total number of H-bonds (5776). Non-intra-base-pair H-bonds were found in A-DNA, B-DNA, DNA-drug complexes, DNA-protein complexes and unusual DNA structures, like tetraplexes, but not in Z-DNA. In DNA-protein complexes the fraction of structures with non-intra-base-pair H-bonds is significantly higher than for the other DNA classes. Less than 50% of the non-intra-base-pair H-bonds are three-center bonds and about 30% are of the base-backbone type. The preferred nucleotide pair is AT, even though all other nucleotide combinations, except for AC, occur as well. This is also correct for the GC interaction in spite of its assumed rigidity due to the three H-bonds. On the other hand, there is a large number of AT sequence ranges which do not show non-intra-base-pair H-bonds at all. Moreover, the great majority of known structures has central AT tracts, which means that the results are biased towards the AT case. Therefore, the assumption that non-intra-base-pair H-bonds in AT tracts are responsible for their particular rigidity is not clearly substantiated. When increasing the cutoff value for the HA distance from 2.5 to 3Å the fraction of non-Z-DNA structures with non-intra-base-pair H-bonds increases from 24% in the first case to 75% in the second one. Finally the distributions of HA distances and DHA angles for all H-bonds in the structure set are reported. These distributions have maxima at HA distances between 1.8 and 1.9 Å and at DHA angles between 160 and 170 °.